

REMARKS

Reconsideration and allowance of the subject application are respectfully requested.

Claims 8, 13, 14, 16-26 and 28-42 are pending in this application. Claims 19, 20, 28-32 and 36-42 stand withdrawn from consideration pursuant to a Restriction Requirement.

Basis for new claims 43-47 can be found in the present specification including at page 13, line 30. No new matter has been added.

Claim 26 has been amended remove reference to $n = 2$. No new matter has been added and these claims have not been amended to overcome prior art. The full doctrine of equivalents applies to each and every claim element.

The rejection of claim 26 under 35 U.S.C. § 112, first and second paragraphs, is respectfully traversed. Claim 26 fully complies with Section 112 for the many reasons of record. Applicants retain the right to pursue the full breadth of claim 26. To further prosecution, claim 26 has been amended to remove reference to $n=2$. Accordingly, withdrawal of the Section 112 rejection is respectfully requested.

The rejection of claims 8, 14, 16-18 and 21-25 under 35 U.S.C. § 103 over Hopp is respectfully traversed. Applicants respectfully submit that the Examiner has not provided a prima facie case of obviousness and even if a prima facie case has been provided, the claimed invention is not obvious from Hopp for the following reasons.

The Examiner states on page 6 of the Office Action that "[a]s has been indicated in the Examiner's Answer, Hopp teaches the claimed compositions and use thereof using active agents of formula I." This simply is not true. The Examiner even admits as much by stating on page 8 of the Office Action that "the prior art [Hopp] active agent differs from what is claimed by only as to the position of the alkyl group on the benzene ring or in a homologous manner." Thus, the Examiner admits that there are differences between Hopp and the claimed invention.

The Examiner argues that the claims recite isomers or homologs of the compounds disclosed in Hopp and differ only by the placement of the alkyl on the benzene ring. By use of the term "isomers" it is believed that the Examiner is referring to "position isomers" which are defined by MPEP 2144.09 as "compounds having the same radicals in physically different positions on the same nucleus." Homologs are defined by MPEP 2144.09 as "compounds differing regularly by the successive addition of the same chemical group, e.g., by $\text{-CH}_2\text{-}$ groups."

Hopp does **not** disclose the use of alkyls substituted on the benzene ring, but rather only the use of **isopropyl** or **tert-butyl**. See column 1, line 39 of Hopp. Thus, the only compounds recited in the claims of the subject application that can be a "position isomer" of the compounds disclosed in Hopp are those in which only one of R_3 , R_4 , R_6 and R_7 is isopropyl or tert-butyl, the remaining groups R_3 through R_7 and R_1 are hydrogen, R_2 is methyl, and n is 1. Furthermore, the only compounds recited in the claims of the subject application which can be a "homolog" of the compounds disclosed in Hopp are those in which R_5 is isopropyl or tert-butyl, all of R_3 , R_4 , R_6 and R_7 are hydrogen, R_2 is methyl, and n is 2. All other compounds recited in the claimed invention cannot be a position isomer or homolog of the compounds disclosed in Hopp.

Homology and isomerism are **not** substitutes for a prima facie case of obviousness and they are only a relevant fact in the determination of obviousness. Even if the Examiner has provided a prima facie case, the experimental evidence of record and submitted herewith rebuts any such prima facie case of obviousness. Claims 8, 14, 16-18 and 21-25 recite novel compounds and compositions which are not disclosed in Hopp. The experimental evidence disclosed in the present specification demonstrates the unexpected advantages of the claimed compounds compared to those disclosed in Hopp. Hopp only discloses that their compounds have a microbicide effect on staphylococcus epidermis and aureus, and candida albicans. In contrast, the claimed compounds and compositions exhibit an unexpected microbicide effect against e-coli (Tables on pages 19, 21, 25, and 27 of the present application), as well as

unexpected anti-fungal properties (Tables on pages 23 and 24 of the present application). Hopp does not teach or suggest that the claimed compounds have anti-fungal properties or microbicide properties against e-coli and therefore cannot make obvious the compounds and compositions recited in claims 8, 14, 16-18 and 21-25.

Applicants respectfully traverse the Examiner's argument that the 'rule' that 'compounds of a homologous series are recognized as possessing a community of properties in common' is accurate. It is known that there is an +I effect (inductive) for aliphats which can give impact in all positions of the benzene ring, but they are superimposed by +/- M (mesomeric) effects, which are active in *o*- and *p*- positions of the benzene ring (for example Cl group with +M and -I effect and C≡N group with -M, -I effect). The theory of +/- I effects and +/- M effects may be known, however, this theory cannot be used to ignore experiments that have uncovered unexpected *activity* of a compound.

In the present application, unexpectedly, the lipophily and topology plays a major role for the biocidal activity of the presently claimed formula I (see attached Rule 132 Declaration), even more than homologue, isomeric or electronic (+/- I, +/- M) effects.

The Examiner even admits that one of ordinary skill in the art would expect that the claimed compositions to have different properties compared to the compositions disclosed in Hopp. See page 15 of the Office Action:

It is further noted, that the assertion of one expecting similar properties in view of the close structural similarity of the instant active agents to those of the prior art is not an assertion of identical properties but rather similar properties. After all the agents are not identical in every respect and one would not expect identical properties.

Applicants submit that the Examiner is unfairly relying on the novel properties of the presently claimed compositions disclosed in the present application for the basis of his Section 103 rejection. The different properties of the present invention, such as anti-fungal properties, are not expected from the Hopp active agents and the Examiner has

provided no evidence to the contrary. For these reasons alone, the Section 103 rejection should be withdrawn.

Applicants respectfully submits that the Examiner's allegations that one of ordinary skill in the art would be motivated to make the claimed compounds is based on unfounded assumptions. The Examiner's reliance on *In re Shetty*, 195 USPQ 753; *In re Lintner*, 173 USPQ 560; and *In re Hoch*, 166 USPQ 406, to support a prima facie case of obviousness and to find obviousness is without merit for the following reasons.

Shetty stated that homologs may give rise to a prima facie case of obviousness since the Appellant did not provide counter arguments. *Shetty*, p 756, held that since the Appellant did not provide any experimental evidence showing actual differences in properties the homologs were obvious, relying on *Hoch*. In contrast to the facts in *Shetty*, present Applicants have demonstrated that the properties of the claimed compounds are actually different and unexpected compared to the properties of the Hopp active agents, as discussed above.

Lintner relates to a laundry composition in which the invention differed from the prior art composition by the reason for the addition of sugar. The prior art disclosed the use of sugar. The court found the presence of sugar for a different reason was not patentable. The court in *Lintner*, at p. 562, stated that:

"In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the references before him to make the proposed substitution, combination or other modification."

The Examiner has not demonstrated how the references teach or provide a suggestion to one of ordinary skill in the art to modify the compounds of Hopp to arrive at the claimed compounds, nor the claimed compositions containing the compounds. Unlike the facts in *Lintner*, the presently claimed compounds and compositions are not disclosed in Hopp, whereas the sugar in *Lintner* was disclosed in the prior art

references. Thus, the Examiner's finding of obviousness based on *Lintner* is without merit and should be withdrawn.

Hoch, p. 409, held that a prima facie case was not overcome because the Appellants did not show how the reference compounds and claimed compounds actually differ in properties. In contrast, in the present Appeal the Appellant has demonstrated that the properties of the claimed compounds and compositions are actually different than those of Hopp, as discussed above. Thus, *Hoch* does not support the Examiner's conclusion that the claimed invention is obvious over Hopp.

For all of the reasons advanced above, the Appellants submit that the claimed invention is not obvious over Hopp and therefore withdrawal of the Section 103 rejection is respectfully requested.

The rejection of claims 8, 13, 14, 16-18, 21-25 and 33-35 under 35 U.S.C. § 103 over U.S. Patent 4,321,257 (Sipos) is respectfully traversed. The claimed invention is not taught or suggested by Sipos for the following reasons.

The Examiner admits that Sipos does not disclose the claimed compounds. See page 15 of the Office Action. The Examiner then argues that the group III phenol alkanols disclosed in Sipos generically teach the claimed compounds and that "[i]t is well within the skill of the artisan to select among the alternatives of the reference to afford compounds possessing the prior art use."

Applicants submit that Sipos teaches that the large list of group III phenol alkanols cited by the Examiner are only "potentiators" (column 4, lines 23 and 55). Potentiators are taught as enhancing the activity of an antimicrobial agent, not that the potentiator is an antimicrobial agent (column 3, lines 15-18). Thus, Sipos does not teach any compounds having the claimed properties such that one can merely select alternatives therefrom as alleged by the Examiner.

In contrast, the presently claimed compounds are antimicrobial agents, disinfectants, deodorants, antimycotics or preservatives, not merely potentiators, as demonstrated by the experimental results disclosed in the Examples of the present specification. Sipos does not teach or suggest that any species in the group III phenol

alkanols would have antimicrobial, disinfectant, deodorant, antimycotic or preservative properties and therefore cannot make obvious use of these compounds as an antimicrobial agent, disinfectant, deodorant, antimycotic or preservative.

Applicants respectfully submit that Examiner's allegations that one of ordinary skill in the art would be motivated to make the claimed compounds from reading Sipos is based on unfounded assumptions. The Examiner again improperly relies on *In re Shetty*, 195 USPQ 753; *In re Lintner*, 173 USPQ 560; and *In re Hoch*, 166 USPQ 406, to support a prima facie case of obviousness and to find obviousness.

Shetty stated that homologs may give rise to a prima facie case of obviousness since the Appellant did not provide counter arguments. *Shetty*, p 756, held that since the Appellant did not provide any experimental evidence showing actual differences in properties the homologs were obvious, relying on *Hoch*. In contrast to the facts in *Shetty*, the present Applicants have demonstrated that the properties of the claimed compounds and compositions containing the compounds are actually different and unexpected compared to properties of the compounds of Sipos. Sipos does not disclose any properties of compounds, which are purported to be similar to the claimed compounds. Furthermore, the claimed compounds are not isomers or homologs of the compounds disclosed in Sipos and therefore *Shetty* does not support the Examiner's conclusion that a prima facie case of obviousness has been presented.

Lintner relates to a laundry composition in which the invention differed from the prior art references by the reason for the addition of sugar. The prior art disclosed the use of sugar. The court found the presence of sugar for a different reason was not patentable. The court in *Lintner*, at p. 562, stated that:

"In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the references before him to make the proposed substitution, combination or other modification."

The Examiner has not demonstrated how the references teach or suggest to one of ordinary skill in the art to modify the compounds of Sipos to arrive at the claimed compounds, nor the specifically claimed compositions containing these compounds. Unlike the facts in *Lintner*, the claimed compounds and compositions are not disclosed in Sipos, whereas the sugar in *Lintner* was disclosed in the prior art references. Thus, the Examiner's finding of obviousness based on *Lintner* is without merit and should be withdrawn.

Hoch, p. 409, held that a prima facie case was not overcome because the Appellant did not show how the reference compounds and claimed compounds actually differ in properties. In contrast, the present Applicants have demonstrated that the properties of the claimed compounds and compositions are actually different than those of Sipos. Thus, *Hoch* does not support the Examiner's conclusion that the claimed invention is obvious over Sipos.

Applicants submit that the present invention is not obvious and that the 'rule' that 'compounds of a homologous series are recognized as possessing a community of properties in common,' as alleged by the Examiner, is not always true. It is not obvious by reading *Sipos* that the activity of the presently claimed compounds depends on (i) topology instead of homology and (ii) the lipophily of structural parts. The claimed structural types provide unexpectedly high activity. The submitted herewith Rule 132 Declaration discloses the MIC values of 11 compounds. There is a conclusive explanation based on topologic arguments and on lipophilic/hydrophilic arguments. The screening results show that the activity of the biocidal alcohol as claimed for formula I can now be explained by a common structure of a lipophilic unit and a hydrophilic OH group that is separated by a (rigid) spacer unit of around 3 to 4 carbon atoms within an aliphatic chain, which has a branch on the beta position to the benzene ring.

For example, the strong impact of lipophilic substituents such as CH₃, C₂H₅ or Cl either at the benzene ring or the alcohol CH₂ chain (compounds 4, 5, 6) compared to 3-phenylpropanol (1) **cannot be explained by isomeric or homologue effects.** The

dialkyl substitution of the spacer chain has the highest impact on the β -position of the aliphatic spacer unit, which is not expected from looking at isomeric effects (compare 2 vs. 1 and k).

In "Supramolecular Chemistry" one can find a lot of examples where topology plays a major role over other electronic and homologue effects and especially over isomery, especially for the chemistry of host guest interactivity. Attached is one literature reference, but there are many more articles if one searches this sector of chemical investigation.

Attached is a translation of R. Berscheid, M. Nieger, F. Vögtle, *Chem. Ber.* **1992**, 125, 2539-2552. This article discloses a triply-bridged dye molecule, its synthesis and solvatochromic and halochromic effects to different isomeric structures in table 7 (page 2542). For example 1,2-dimethylbenzene exhibited a significant shift in UV spectra while 1,4-dimethylbenzene does not. This effect is explained by sterical reasons and the topology of the molecule. The 1,2-dimethylbenzene fits to the host structure while the 1,4-isomer does not. This article demonstrates that the simple view of isomers having similar activity is not always true.

The Examiner's statement on page 23 of the Office Action "[t]hat is one would expect to obtain additional active agents having the prior art use by such a modification of the prior art" is without basis. The Examiner's circular argument fails for the simple reason that Sipos does not teach any compounds having any of the claimed properties and, thus, there can be no such additional active agents suggested by Sipos.

For all of the reasons advanced above, Applicants submit that the claimed invention is not obvious over Sipos and therefore withdrawal of the Section 103 rejection is respectfully requested.

The rejection of claim 26 under 35 U.S.C. § 103 over U.S. Patent 4,968,668 (Hafner) in view of Vogel, "A Textbook of Practical Organic Chemistry" is respectfully traversed. Applicants submit that claims 26 is not taught or suggested by the theoretical combination of Hafner and Vogel for the following reasons.

The Examiner admits that Hafner does not teach the claimed step (a) and that some of the reactants differ as to the substituents present. The Examiner argues that Vogel teaches the claimed step (a).

There is no motivation in either of the cited references to follow the claimed step (a) to form the specific monoalkylated malonic acid alkyl esters claimed and then follow the claimed steps (b) through (d) to form the specific alcohols presently claimed. Applicants respectfully submit that the Examiner is unfairly relying on hindsight gleaned from the present specification and is improperly using the present specification as a blueprint to piece unrelated teachings from the references together.

The Examiner admits that Hafner uses different reactants and thus forms different products than those presently claimed. The Examiner merely argues that the use of a new starting material in an otherwise old process is considered obvious and improperly cites cases as the only basis for the rejection. The Appellant directs the Examiner's attention to *In re Ochiai*, 37 USPQ2d 1127, 1132 (Fed. Cir. 1995), in which the Federal Circuit stated that:

"Mere citation of *Durden*, *Albertson* or any other case as a basis for rejecting process claims that differ from the prior art by their use of different starting materials is improper, as it sidesteps the fact-intensive inquiry mandated by Section 103."

The Examiner has provided no motivation or teaching in any of the cited references which would direct one of ordinary skill in the art to ignore the teachings in Hafner and use different reactants (as presently claimed) and then change the process of Hafner and use part of the method disclosed in Vogel.

The Examiner improperly relies on *In re McLaughlin*, 170 USPQ 209 to support a prima facie case of obviousness. *McLaughlin* relates to a mechanical invention in which a reference teaching boxcars is combined with a reference teaching a side filler panel. The Examiner is relying on the statement "any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning" to support his prima facie case. However, the Examiner must still demonstrate that some teaching in

the prior art provides the motivation to combine the teachings. The Federal Circuit stated in *Uniroyal Inc. v. Rudkin-Wiley Corp.*, 5 USPQ2d 1434, 1438 (Fed. Cir. 1988) that:

When prior art references require selective combination . . . to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself . . . Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination.

Applicants submits that the Examiner has not provided any teaching or suggestion in the prior art which provides any motivation to selectively combine Hafner and Vogel.

For these reasons, Applicants respectfully submit that the Examiner has not provided sufficient evidence to support a prima facie case of obviousness and the Section 103 rejection should be withdrawn for this reason alone.

Even if the references were combined, the theoretical combination of Hafner and Vogel would not make obvious the method recited in claim 26. The theoretical combination of Hafner and Vogel provides a method which makes a different alcohol than those claimed because Hafner teaches the use of different reactants than those in the claimed method.

Furthermore, the claimed invention provides unexpected properties not disclosed in the cited references. As discussed above, the compounds formed by the claimed method exhibit antimicrobial, disinfectant, deodorant, antimycotic or preservative properties. Hafner only discloses that the alcohols disclosed therein provide fragrance properties. Vogel also does not teach or suggest a method of forming compounds that are suitable for use as antimicrobial, disinfectant, deodorant, antimycotic or preservative agents.

For these reasons, the claimed method is not taught or suggested by the theoretical combination of Hafner and Vogel. Accordingly, withdrawal of the Section 103 rejection is respectfully requested.

Applicant further maintains that the prior art rejections should be withdrawn for non-compliance with MPEP § 706.04. MPEP § 706.04 provides that great care should be exercised in authorizing a rejection of a previously allowed claim. Full faith and credit should be given to the search and action of the previous Examiner unless there is a clear error in the previous action or knowledge of other prior art. In general, an examiner should not take an entirely new approach or attempt to reorient the point of view of a previous Examiner, or make a new search in the mere hope of finding something.

In paragraph 14, on page 7 of the first Office Action dated October 3, 1997, Examiner Puttlitz stated that the subject matter of claims 9 and 10 was allowable. Original claim 5 was not rejected over prior. Present independent claim 13 recites the subject matter of original claim 5. Present independent claim 14 recites the subject matter of allowed claim 9. Present claim 15 recites the subject matter of allowed claim 10. All of the independent claims of record include a compound which was held to be patentable over the prior art by original Examiner Puttlitz.

New Examiner Shippen has improperly withdrawn the allowability of claims 9 and 10 and rejected the subject matter of allowed claims 9 and 10 and claim 5 under the guise of newly found prior art. The alleged newly found prior art is farther removed from the claimed invention than the references cited by the original Examiner Puttlitz.

Present Examiner Shippen admits that the new prior art does **not** disclose the claimed compounds. Examiner Shippen relies on the very rarely used doctrine of "structural similarity" to reject the claimed invention over the newly cited references.


Present Examiner Shippen improperly conducted a new search and has improperly taken an entirely new approach to reorient the point of view of previous Examiner Puttlitz. As discussed more fully below, new Examiner Shippen improperly stretches the teachings in the alleged new prior art and relies on the very weak doctrine of "structural similarity". The new search and new approach do not comply with the requirements of MPEP § 706.04, and therefore the prior art rejections of record should be withdrawn for this reason alone.

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In view of all of the rejections of record having been addressed, Applicant submits that the present invention is condition for allowance and Notice to that effect is respectfully requested.

Respectfully submitted,

Manelli, Denison & Selter, PLLC

By 
Jeffrey S. Melcher
Reg. No.: 35,950
Tel. No.: (202) 261-1045
Fax. No.: (202) 887-0336

Customer No. 20736